AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1.   (Original) A method of determining a likelihood of a fetus carried by a pregnant mother having a chromosomal abnormality, a first biological, parameter being suitable for screening said fetus for said chromosomal abnormality, the method comprising:

receiving first data from a first stage of pregnancy of said mother, said first data comprising data representing a first value of said first biological parameter;

receiving second data from a second, later stage of said pregnancy, said second data comprising data representing a second value of said first biological parameter; and

determining likelihood data from said first and second data, said likelihood data representing the likelihood of said fetus having a chromosomal abnormality.

2.   (Original) A method as claimed in claim 1 wherein said first biological parameter is a marker for said chromosomal abnormality at one of said first and second stages of pregnancy and has substantially no value as a marker during the other of said first and second stages of pregnancy.

3.   (Original) A method as claimed in claim 1 wherein said first biological parameter has a logarithm multiple of median (log MoM) value closer than one standard deviation to zero.

4.   (Currently amended) A method as claimed in claim 1, ~~2 or 3~~ wherein in a cohort of pregnancies having said abnormality said first biological parameter is selected such that a correlation coefficient of said first and second values of said parameter is greater than 0.3, preferably greater than 0.5, more preferably greater than 0.6, most preferably greater than 0.8.

5.   (Currently amended) A method as claimed in <u>claim 1</u> any one of claims 1 to 4 wherein said first biological marker comprises one of total hCG, PAPP-A, Inhibin – A, AFP, uE₃.

6.   (Currently amended) A method as claimed in <u>claim 1</u> any one of claims 1 to 4 wherein said first biological marker is not free β-LCG.

7.   (Currently amended) A method as claimed in any preceding claim <u>1</u> wherein said first data further comprises data representing a first value of a second biological parameter, wherein said second data further comprises data representing a second value of said second biological parameter, wherein said second biological parameter is suitable for screening said fetus for said chromosomal abnormality.

8.   (Original) A method as claimed in claim 7 wherein said second biological parameter is a marker for said chromosomal abnormality at one of said first and second stages of pregnancy and has substantially no value as a marker during the other of said first and second stages of pregnancy.

9.   (Currently amended) A method as claimed in claim 7 or 8 wherein in a cohort of pregnancies having said abnormality biological parameter is selected such that a correlation coefficient of said first and second values of said parameter is greater than 0.3, preferably greater than 0.5, more preferably greater than 0.6, most preferably greater than 0.8.

10.   (Currently amended) A method as claimed in claim 7, 8 or 9 wherein said second biological marker comprises on of total hCG, PAPP-A, Inhibin – A, AFP, uE₃.

11.   (Currently amended) A method as claimed in claim 7, 8 or 9 wherein said second biological marker is not free β-LCG.

12.   (Currently amended) A method as claimed in any preceding claim <u>1</u> wherein said first data further comprises data obtained from an ultrasound scan performed on said mother.

13. (Currently amended) A method as claimed in ~~any preceding~~ claim 1 wherein said determining of said likelihood data comprises determining likelihood ratio data, said likelihood ratio data comprising a ratio of a probability of obtaining said first and second data in a pregnancy without said abnormality to a probability of said first and second data being obtained in a pregnancy in which said fetus has said abnormality.

14. (Original) A method as claimed in claim 13 further comprising adjusting said first and second data responsible to one or more covariates prior to determining said likelihood ratio.

15. (Currently amended) A method as claimed in claim 13 ~~or 14~~ further comprising adjusting said likelihood ratio by a prior probability factor dependent upon an age of said mother.

16. (Currently amended) A method as claimed in <u>claim 1</u> ~~any one of claims 1 to 15~~ wherein said first stage of pregnancy comprises a first trimester of said pregnancy and said second stage of said pregnancy comprises a second trimester of said pregnancy.

17. (Currently amended) A method as claimed in <u>claim 1</u> ~~any one of claims 1 to 15~~ wherein said first stage of pregnancy comprises a stage of said pregnancy from 8 to 13 weeks, and wherein said second stage of said pregnancy comprises a stage of said pregnancy from 14 to 22 weeks.

18. (Currently amended) A method as claimed in ~~any preceding~~ claim 1 wherein said fetus is a human fetus.

19. (Currently amended) A method as claimed in ~~any preceding~~ claim 1 wherein said chromosomal abnormality comprises Down's Syndrome.

20. (Original) A method of determining whether a pregnant woman is at an increased risk of having a fetus with Down's Syndrome, the method comprising the steps of:

measuring at least one screening marker level from one of a first and second stage of pregnancy by assaying a sample obtained from the pregnant woman at said first or second stage of pregnancy for at least one biochemical screening marker;

measuring a level of the same said at least one screening marker at the other of said first and second stage of pregnancy by assaying a sample obtained from the pregnant woman at said other stage of pregnancy for said at least one biochemical screening marker; and

determining a quantitative estimate of the risk of Down's Syndrome using the measured screening marker levels from both the first and second stages of pregnancy.

21.   (Original) A method of determining whether a pregnant woman is at an increased risk of having a fetus with Down's Syndrome, the method comprising the steps of:

measuring at least one screening marker level from one of a first and second stage of pregnancy by assaying a sample obtained from the pregnant woman at said first or second stage of pregnancy for at least one biochemical screening marker;

determining a first quantitative estimate of the risk of Down's syndrome using said measured screening marker level from the first stage of pregnancy;

measuring a level of the same said at least one screening marker at a second stage of pregnancy by assaying a sample obtained from the pregnant woman at said second stage of pregnancy for said at least one biochemical screening marker; and

determining a quantitative estimate of the risk of Down's Syndrome using the measured screening marker levels from both the first and second stages of pregnancy.

22.   (Currently amended) A method as claimed in claim 20 ~~or 21~~ wherein said at least one biochemical screening marker is a marker at one of said first and second stages of pregnancy but not at the other.

23.   (Currently amended) A method as claimed in claim 20~~, 21, or 22~~ wherein said measured screening marker levels from said first and second stages of pregnancy are highly correlated with one another.

24. (Currently amended) A method as <u>claimed in claim 20</u> ~~any one of claims 20 to 23~~ further comprising:

measuring a second screening marker level from one of said first and second stage of pregnancy by:

assaying a sample obtained from the pregnant woman at said first or second stage of pregnancy for ~~said~~ a second biochemical screening marker;

measuring a level of said second screening marker at the other of said first and second stage of pregnancy by:

assaying a sample obtained from the pregnant woman at said other stage of pregnancy for said second biochemical screening marker; and

wherein said determining determines said Down's risk estimate further using the measured second screening marker levels from both said first and second stages of pregnancy.

25. (Original) A method as claimed in claim 24 wherein said second biochemical screening marker is a marker at one of said first and second stages of pregnancy but not at the other.

26. (Currently amended) A method as claimed in claim 24 ~~or 25~~ wherein said measured second screening marker levels from said first and second stages of pregnancy are highly correlated with one another.

27. (Currently amended) A method as claimed in <u>claim 20</u> ~~any one of claims 20 to 26~~ further comprising:

measuring at least one ultrasound screening marker from an ultrasound scan taken at one of said first and second stages of pregnancy; and

wherein determining determines said Down's risk estimate further using said ultrasound screening marker.

28. (Currently amended) <u>A carrier carrying</u> processor control code to, when running, implement the method of <u>claim 1</u> ~~any one of claims 1 to 19~~.

29.   (Currently amended) A carrier carrying the processor control code to, when running, implement the method of claim 20 [[28]].

30.   (Original) A computer program to, when running, determine a pregnant woman's risk of having a fetus with Down's syndrome, the computer comprising code to:

input measurement data from a measurement of at least one screening marker level from one of a first and second stage of pregnancy obtained by assaying a sample obtained from the pregnant woman at said first or second stage of pregnancy for at least one biochemical screening marker;

input measurement data from a measurement of a level of the same said at least one screening marker at the other of said first and second stage of pregnancy obtained by assaying a sample obtained from the pregnant woman at said other stage of pregnancy for said at least one biochemical screening marker; and

determine a quantitive estimate of the risk of Down's syndrome using the measured screening marker levels from both the first and second stages of pregnancy.

31.   (Cancelled)

32.   (Original) A computer system for providing risk data representing a likelihood of a fetus carried by a pregnant mother having a chromosomal abnormality, a first biological parameter being suitable for screening said fetus for said chromosomal abnormality, the computer system comprising:

a data store operable to store data to be processed;

an instruction store storing processor implementable instructions; and

a processor coupled to said data store and to said instruction store and configured to load and implement said stored instructions, said instructions comprising instructions for controlling the processor to:

input first data from a first stage of pregnancy of said mother, said first data comprising data representing a first value of said first biological parameter;

input second data from a second, later stage of said pregnancy, said second data comprising data representing a second value of said first biological parameter;

determine said risk data from said first and second data; and

output said determined risk data.

33.   (New) A method as claimed in claim 21 wherein said at least one biochemical screening marker is a marker at one of said first and second stages of pregnancy but not at the other.

34.   (New) A method as claimed in claim 21 wherein said measured screening marker levels from said first and second stages of pregnancy are highly correlated with one another.

35.   (New) A method as claimed in claim 21 further comprising:

measuring a second screening marker level from one of said first and second stage of pregnancy by:

assaying a sample obtained from the pregnant woman at said first or second stage of pregnancy for said a second biochemical screening marker;

measuring a level of said second screening marker at the other of said first and second stage of pregnancy by:

assaying a sample obtained from the pregnant woman at said other stage of pregnancy for said second biochemical screening marker; and

wherein said determining determines said Down's risk estimate further using the measured second screening marker levels from both said first and second stages of pregnancy.

36.   (New) A method as claimed in claim 35 wherein said second biochemical screening marker is a marker at one of said first and second stages of pregnancy but not at the other.

37.   (New) A method as claimed in claim 35 wherein said measured second screening marker levels from said first and second stages of pregnancy are highly correlated with one another.

38.   (New) A method as claimed in claim 21 further comprising:

measuring at least one ultrasound screening marker from an ultrasound scan taken at one of said first and second stages of pregnancy; and

wherein determining determines said Down's risk estimate further using said ultrasound screening marker.

39.   (New) A carrier carrying processor control code to, when running, implement the method of claim 21.